ORSETT BRIEFING PAPERS FOR PSYCHOLOGISTS

NO.17 - STROKE, DEPRESSION AND SLEEP

INTRODUCTION

A stroke is when the blood supply to the brain is blocked or when a blood vessel in the brain ruptures, causing brain tissue to die [1].

Types

1. Ischemic stroke - the artery supplying blood to the brain is blocked by blood clots, for example, and this causes damage to brain tissue.

2. Haemorrhagic stroke - the artery in the brain leaks, and blood puts pressure on the brain causing damage.

3. Transient ischemic attack ("mini-stroke") [2].

STROKE AND DEPRESSION

A number of individuals experience depression after stroke. For example, 31% of individuals at three months post-stroke and 29% at three years in a Swedish study [3], and 43% at six months and 18% at three years in another study [4]. One in three stroke survivors experience depression according to a review of fifty-one observational studies (between 1977 and 2002) [5]. The studies all involved consecutive patient recruitment.

Outside the West, a similar level of post-stroke

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[1] http://www.cdc.gov/stroke/ (accessed 12/03/2014).
[2] http://www.cdc.gov/stroke/types_of_stroke.htm (accessed 12/03/2014).
[3] Astrom, M et al (1993) Major depression in stroke patients: A three-year longitudinal study Stroke 24, 976-982.
[4] Verdelho, A et al (2004) Depressive symptoms after stroke and relationship with dementia: A three-year follow-up study Neurology 62, 905-911.
[5] Hackett, M.L et al (2005) Frequency of depression after stroke: A systematic review of observational studies Stroke 36, 1330-1340.

depression was found in an Indian study [6]. Just over one-third of 241 stroke survivors 8-12 months later in Kolkata between 2006 and 2010 [7]. But a study of older stroke survivors in rural China found depression in close to two-thirds of them [8].

The variation in rates of depression depend on how depression is measured [9]. For example, two studies using a single simple question to establish depression had an average rate of 14%, whereas studies using structured questionnaires estimated rates of 26-41% [10]. One study using both a self-report measure (Beck Depression Inventory) and a diagnostic interview (Present State Examination) found different rates - 20% and 11% respectively [11].

Some studies have control groups. For example, the Framingham Study [12], which is an ongoing observational study of middle-aged adults in a US community, compared stroke victims between 1982 and 1994 with matched controls. The rate of depression six months post-stroke was 38% compared to 10% of controls [13]. This is a statistical significant difference.

There are three key issue related to depression after stroke:

(a) The relationship between stroke and depression.

In a Swedish hospital, major depression was more common in individuals with left hemisphere than right hemisphere stroke (14 of 21 vs 2 of 23), and left-anterior than left-posterior damage (12 of 14 vs 2 of 7) [14].

The different symptoms of depression vary over time. For example, sadness, slowness, and concentration difficulties were evident after six months, but only

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[6] Paul, N et al (2013) Depression among stroke survivors: A community-based, prospective study from Kolkata, India American Journal of Geriatric Psychiatry 21, 821-831.

[7] This study also showed differences in depression based on income/area lived - eg: 39% (slum dwellers - poor) versus 25% (high-rise apartment in centre of city - rich).

[8] Fuh, J.L et al (1997) Post-stroke depression among the Chinese elderly in a rural community Stroke 28, 1126-1129.

[9] Hackett et al's (2005) review found ten different self-report or interviewer-administered scales (eg: Beck Depression Inventory, Hamilton Depression Rating Scale, Zung Depression Inventory), and four different diagnostic interview schedules. Studies also varied in their cut-off for defining depression when using the same rating scale.

[10] op cit Hackett et al.

[11] House, A et al (1991) Mood disorders in the year after first stroke British Journal of Psychiatry 158, 83-92.

[12] Details at http://www.framinghamheartstudy.org/.

[13] Kase, C.S et al (1998) Intellectual decline after stroke: The Framingham Study Stroke 29, 805-812.

[14] op cit Astrom et al.

sadness remained at twelve months. Slowness and concentration difficulties remained at three years, however, in individuals with dementia [15]. About one-third of stroke survivors suffer from dementia [16].

(b) The risk factors for those who develop post-stroke depression.

i) Pre-stroke - Living alone as opposed to with someone (12 of 30 vs 7 of 46 patients) [17]. Family history and/or prior personal experience of anxiety and/or depression; greater neuroticism; more recent negative life events; being male; older at time of stroke [18].

An Indian study found that depression was associated with being older at the time of stroke, and subsequently having greater disability, but no relationship to gender, or location of damage in the brain [19].

ii) Post-stroke - Dependent on others for activities of daily living (ie: greater disability) [20]. Fewer social contacts was the strongest predictor of depression at three years post-stroke [21].

c) The effect of depression on stroke recovery.

Post-stroke depression is associated with mortality. For example, a follow-up of over one hundred acute stroke patients ten years later found that individuals with immediate post-stroke depression (ie: while still recovering from stroke in hospital) were over three times more likely to have died than non-depressed patients. Depressed individuals with few social contacts were at the highest risk [22].

The North East Melbourne Stroke Incidence (NEMESIS) found that anxiety and depression independently contribute to stroke outcome at two years [23]. This study involved all cases of first-ever stroke between 1st May 1998 and 30th April 1999 among residents in the north and east suburbs of Melbourne in Australia, and followed-up

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[15] op cit Verdelho et al.
[16] Altieri, M et al (2005) Update on stroke Current Opinion in Psychiatry 18, 331-334.
[17] op cit Astrom et al.
[18] Castillo, C.S & Robinson, R.G (1994) Depression after stroke Current Opinion in Psychiatry 7, 87-90.
[19] op cit Paul et al.
[20] op cit Castillo & Robinson .
[21] op cit Astrom et al.
[22] Morris, P.L.P et al (1993) The association of depression with ten-year post-stroke mortality American Journal of Psychiatry 150, 124-129.
[23] Sturm, J.W et al (2004) Quality of life: The North East Melbourne Stroke Incidence Study (NEMESIS) Stroke 35, 2340-2345.

two years after stroke. Two hundred and sixty-six individuals were found/alive at the time (of 516 cases). The purpose of the study was to assess health-related quality of life (HRQoL). Poorer HRQoL was reported by women, older individuals, institutionalised individuals, those with low socio-economic status, depression sufferers, and individuals with greater disability. The rating of HRQoL "suggests that people in the general community would rather give up half of their remaining years of life to live in full health than continue living with the health status of the average stroke survivor" [24].

Recurrent stroke occurs in around one in ten survivors of the first stroke [25]. Depression after the first stroke increases the risk of subsequent stroke. A recent study in China found a one and half times increase of risk of recurrent stroke within one year among individuals with post-stroke depression than post-stroke non-depressives [26]. Over 1700 patients from fifty-six hospitals were studied between April 2008 and 2010. Depression was diagnosed at two weeks post-stroke using DSM-IV criteria, and recurrent stroke was assessed at 3, 6, and 12 months after the first stroke. Overall, 28% of the sample were depressed (n = 481), and 12% of them had recurrent stroke (n = 58) (compared to 8% of non-depressed patients; 100 of 1232).

Depression Causing Stroke?

Looking at the relationship between stroke and depression differently, does depression increase the risk of future stroke? This was found in the INVADE study [27] in Bavaria, Germany. Pre-stroke depression increased the risk of stroke, particularly among women and 55-64 year-olds (as compared to over 65s). Put together, women in the younger age group who were depressed at baseline had over three times greater risk of a subsequent stroke than non-depressed individuals [28]. Depression was assessed with the Geriatric depression scale (GDS) [29], which has fifteen items (each answered yes or no) related to the previous week (eg: "Do you feel that life is empty?"; "Do you feel

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[24] ibid p2343.

[25] Yuan, H.W et al (2012) Post-stroke depression and risk of recurrent stroke at one year in a Chinese cohort study PLoS ONE 7, 10, e46906.

[26] ibid.

[27] Intervention project on cerebrovascular diseases and dementia in the district of Ebersberg.

[28] Seifert, C et al (2012) Depressive symptoms and the risk of ischemic stroke in the elderly - the influence of age and sex PLoS ONE 7, 11, e50803.

[29] Yesavage, J.A et al (1982) Development and validation of a geriatric depression screening tool: A preliminary report Journal of Psychiatric Research 17, 1, 37-49.

that your situation is hopeless?"). A score of five or more was classed as depression. There was a follow-up of six years to see who had suffered a ischemic stroke.

A meta-analysis of 28 prospective cohort studies (up to May 2011) found that depression did significantly increase the risk of stroke and death from stroke. The risk was about one and a half times greater than for non-depressed individuals [30].

For inclusion in the meta-analysis, the studies had to follow-up a cohort of non-institutionalised adults, and compare stroke rates in depressed and non-depressed individuals. In total, there were over 300 000 participants, and over 8000 stroke events, mostly in the USA and Europe. The follow-up period varied from two to 29 years. Depression was mainly self-reported using different scales.

Using the case-control method (retrospective), the INTERSTROKE study found a similar level of risk. Self-reported depression for two or more weeks in the last year was associated with a significantly increased risk of stroke among 3000 cases and 3000 matched controls in twenty-two countries [31].

The severity of depression also increases the risk of stroke (eg: over twice the risk with high depressive symptoms [32]).

How might depression lead to stroke? One answer is via changes in physiology. For example, depression can suppress the immune system, and affect the hypothalamic-pituitary-adrenal axis, which, in turn, can influence stroke risk. Another answer is through poor health behaviours when depressed (eg: poor diet, smoking), which are risk factors for stroke [33].

SLEEP AND STROKE

The average length of time that an individual sleeps each night (sleep duration) is a potential risk factor for stroke, either long (≥9 hours) or short (<6 hours) sleep duration [34]. Compared to 7-8 hours per night

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[30] Pan, A et al (2011) Depression and the risk of stroke morbidity and mortality: A meta-analysis and systematic review Journal of the American Medical Association 306, 11, 1241-1249.

[31] O'Donnell, M.J et al (2010) Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study Lancet 376, 112-123.

[32] Simonsick, E et al (1995) Depressive symptomatology and hypertension-associated morbidity and mortality in older adults Psychosomatic Medicine 57, 5, 427-435.

[33] op cit Pan et al.

[34] Ruiter Petrov, M.E et al (2014) Self-reported sleep duration in relation to incident stroke symptoms: Nuances by body mass and race from the REGARDS Study Journal of Stroke and Cerebrovascular Diseases 23, 2, e123-e132.

sleepers, long sleepers had a 15% greater risk of developing or dying from stroke, and short sleepers a 65% greater risk [35]. "Over the past few decades, self-reported sleep duration in the general population has steadily decreased. The decline is primarily occurring among full-time employed individuals. Therefore, full-time workers with shortened sleep hours may be at increased risk for stroke compared with the general population, which over time may become a greater public health problem" [36].

The relationship between sleep duration and stroke is often confounded by obstructive sleep apnea (OSA) (eg: snoring) [37], which in turn is associated with another confounder, being overweight or obese [38]. The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study controlled for these variables, and found that short sleep duration was a risk for stroke [39].

The REGARDS Study in the USA is a national longitudinal study of non-Hispanic Black and White adults aged 45 and over at baseline (2003). Ruiter-Petrov et al (2014) concentrated on a sub-sample of 5666 employed individuals in 2008, of which about half lived in the "Stroke Belt". This is a term used for eight states [40] with higher than average stroke mortality in the USA.

Sleep duration was self-reported and categorised as <6 hours, 6-6.9 hours, 7-7.9 hours (used as reference group), 8-8.9 hours, and ≥9 hours per night. OSA was assessed at baseline to include snoring, daytime sleepiness, and body mass index (BMI). Six stroke symptoms were self-reported - painless hemibody weakness [41]; painless hemibody numbness; loss of vision in one or both eyes; loss of hemifield vision; inability to understand; inability to express self verbally or in writing [42]. The participants were telephoned every six months over approximately three years [43].

Four hundred and ten participants were categorised as short sleepers (<6 hours per night), 2216 participants as the reference group (7-7.9 hours), and 334 as long sleepers (≥9 hours). Generally, short sleepers were more likely to be obese, Black, or male, while long sleepers were heavy alcohol consumers. Both extremes were also

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[35] Cappuccio, F.P et al (2011) Sleep duration predicts cardiovascular outcomes: A systematic review and meta-analysis of prospective studies European Heart Journal 32, 1484-1492.
[36] op cit Ruiter Petrov et al p e124.
[37] Information at http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001814/.
[38] op cit Ruiter Petrov et al.
[39] op cit Ruiter Petrov et al.
[40] Alabama, Alaska, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, and Tennessee.
[41] Hemibody = one side of the body.
[42] op cit Ruiter Petrov et al p e125.
[43] Range of study from baseline to final follow-up varied between 751 and 1110 days.

lower income, more depressed, older, had poorer diet, and were smokers, for example, than the reference group.

Ignoring all other variables (ie: unadjusted analysis), there was a significant relationship between short and long sleepers, and reporting stroke symptoms [44]. After controlling for variables including OSA and BMI, there was a significant association between short sleep and stroke symptoms for individuals with normal weight only and low risk of OSA. These individuals had a four times greater risk of stroke symptoms than the reference group [45].

There was no significant association for long sleepers after adjusting for variables. It could be that "long sleep duration as a risk factor for stroke may actually be confounded by the presence of OSA or some other chronic illness that routinely affects the quality of the sleep period. OSA, for example, is associated with sleep fragmentation that contributes to daytime sleepiness and, perhaps, increased physiological sleep need. Therefore, OSA itself rather than long sleep duration may be primarily associated with incident stroke symptoms" [46].

In terms of the physiological mechanism between short sleep and stroke, sleep deprivation is known to affect the immune system (eg: induce inflammation), blood pressure (dysregulate), and other metabolic processes (eg: hormones), which could compromise the cardiovascular system and increase the risk of stroke [47].

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[44] Overall, 283 stroke symptoms were reported. The most common were inability to understand others (21.9%), and loss of vision in one or both eyes (20.1%).

[45] The methodology of this study can be evaluated in the following way:

- Sleep duration was self-reported (ie: no independent verification), and retrospectively (ie: for past six months).
- Only employed individuals, but no controlling for type of work or level of stress.
- Self-reported stroke symptoms rather than "stroke event".

[46] op cit Ruiter Petrov et al pp e129-130.

[47] ibid.

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